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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/556,440	04/24/2000	Ruth A. Gjerset	INRP:032-2	7465

7590 11/18/2002

Steven L Highlander
Fulbright & Jaworski L L P
600 Congress Avenue
Suite 2400
Austin, TX 78701

EXAMINER	
NICKOL, GARY B	
ART UNIT	PAPER NUMBER
1642	13

DATE MAILED: 11/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/556,440	GJERSET, RUTH A.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears n the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 6-26* is/are pending in the application.

4a) Of the above claim(s) *10-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-9 and 18-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

Applicant's response (Paper No. 12) to the Office Communication (Paper No. 11) of July 9, 2002 is acknowledged. Applicant's signed declaration and the cited reference of Martin, N. is of record. Thus, the amendment filed April 4, 2002 (Paper No. 19) in response to the Office Action of October 24, 2001 (Paper No. 8) is acknowledged and has been entered.

Claims 1, and 6-26 are pending.

Claims 10-17 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 1, 6-9, and 18-26 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

New Rejections/Objections:

Specification

The specification is objected to on page 56 for improper disclosure of nucleotide sequences without a respective sequence identifier, i.e. a SEQ ID NOs:. Hence, the disclosure fails to comply with the requirements of 37 CFR 1.821 through 1.825. In the absence of a sequence identifier for each sequence, Applicant must provide a computer readable form (CRF)

copy of the sequence listing, an initial or substitute paper copy of the sequence listing, as well as any amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e-f) or 1.825(b) or 1.825(d). See attached Notice to Comply.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 6-9, and 18-26 are rejected under 35 U.S.C. 102(e) as being anticipated by Roth *et al.*(US Patent No. 6,069,134, April 25, 1994) as evidenced by Jones *et al.* (Mutation Research, DNA Repair, 1991, Vol. 255, pages 155-162)

The claims are drawn to a method for the induction of p53-mediated apoptosis in a cell comprising the steps of (a) introducing into said cell an expression construct comprising a

nucleic acid segment encoding p53 and a promoter operably linked to said nucleic acid segment, and (b) contacting said cell with at least one inhibitory agent that inhibits DNA repair (Claim 1); wherein said expression construct is an adenoviral expression construct (Claim 6); wherein said adenoviral expression construct lacks a portion of at least one gene essential to adenoviral replication (Claim 7); wherein the essential gene is E1 (Claim 8); wherein said promotor is a cytomegalovirus (CMV) promotor (Claim 9); wherein said cell is a tumor cell (Claim 18); wherein said tumor cell is selected from the group consisting of lung, prostate, breast, colon, liver, etc. (Claim 19); wherein said tumor cell is selected from the group consisting of squamous cell carcinoma, non-squamous, glioblastoma, sarcoma, melanoma, etc. (Claim 20); wherein said tumor cell is in a human subject (Claims 21-22); wherein said inhibitory agent is delivered by direct intratumoral injection (Claim 23); wherein said expression construct is delivered by direct intratumoral injection (Claim 24); wherein said injection comprises continuous perfusion (Claims 25-26).

Roth *et al.* teach a method of treating a human subject wherein said subject has cancer (including lung, breast, colon; column 7, lines 45+) further including squamous carcinomas (column 13, line 33), sarcomas, or melanomas (column 38, lines 34+) comprising introducing into said cell an expression construct comprising a nucleic acid segment encoding p53 and a promoter operably linked to said nucleic acid segment, and contacting said cell with at least one inhibitory agent that inhibits DNA repair wherein said expression construct is an adenoviral expression construct (abstract, and column 6, lines 40+) wherein said adenoviral expression construct lacks a portion of at least one gene essential to adenoviral replication (Column 6, line 66); wherein the essential gene is E1 (Column 7, lines 1+; column 15, lines 38+); wherein said

promotor is a cytomegalovirus (CMV) promotor (column 6, line 55). Roth *et al.* further teach that the inhibitory agent and expression construct are delivered by direct intratumoral injection (see claims 7 and 56 of patent) or as continuous perfusions (column 30, line 54).

Roth *et al.* further teach that p53 may be used in combination with a chemotherapeutic agent such as camptothecin (column 9, line 26). As evidenced by Jones *et al.*, campthothecin is "an inhibitory agent that inhibits DNA repair" wherein campthotecin inhibits topoisomerase I (abstract; Table 2, page 159; and page 160, 2nd column, 3rd paragraph). Further, the specification teaches (page 4, lines 21+; page 13, lines 1+) that topoisomerase I is a DNA repair enzyme.

All other rejections and or objections are withdrawn in view of applicant's amendments or arguments there to.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
November 15, 2002

Application 09/556440

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [ ] 7. Other:

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
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